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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,684	GILL, PARKASH S.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 29-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed July 7, 2003 is acknowledged. The application is now in compliance with37 C.F.R. 1.821-1.825.

Claims 1-52 are pending.

Claims 24-28, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1-23 and 29-52 are examined on the merits.

2. The references listed in the Information Disclosure Statements filed 2/13/2002 and Jan 29, 2003 have been considered. References C1-C6 (C7 is a duplicate citation) and C8 of the Information Disclosure Statement filed 2/3/2003 have not been considered because the parent file is not available. Applicant is invited to supply copies of the missing references.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-23 and 29-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 and 29-39 of U.S. Patent No. 6,500,431. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed inventions of U.S. Patent 6,500,431 claim a species that is encompassed by the genus claims of the instant application, or because the claims of the instant application claim an obvious species of the claims of U.S. Patent 6,500,431. Claims 1-6, and 8-10 are anticipated by claims 29-31 of U.S. Patent 6,500, 431. Claim 1 of U.S. Patent 6,500,431 recite methods using polypeptides of almost the same scope as 11-23, and methods that are almost the same scope as methods of 29-36 of the instant application. Claims 37-39 are anticipated by the pharmaceutical compositions of claims 30-39 of U.S. Patent 6,500,431. Claims 40-52, drawn to fusion proteins that comprise the polypeptide used in the method claims of claim 1 of U.S. Patent 6,500,431.

Claim Objections

4. Claims 7-9 and 11-22 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 appears to be at most 71 amino acids in length, whereas claim 7, which is dependent from claim 1, appears to be at least 518 amino acids in length. Claim 8 appears to be at least 518 Claims 9 and 11-22 appear to include peptides that may be 80 amino acids in length.

5. Claims 38 and 39 are objected to under 37 CFR 1.75(b), as being duplicate claims. Applicant is required to cancel or amend the claims.

Claim Rejections - 35 USC § 112

6. Claims 29-36 and 45-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite because the phrase "said organism" lacks antecedent basis.

Claim 45 is indefinite because the phrase "said cell targeting moiety" lacks antecedent basis.

7. Claims 1-3, 5-8, 10, 40-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides comprising the sequence DVCQD (SEQ ID NO: 28), where the polypeptide has anti-angiogenic acitivity, does not reasonably provide enablement for polypeptides comprising the sequence DXCXD, where X is any amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3 and 6-8 are drawn to polypeptides comprising the sequence DX_1CX_2D, where X_1 or X_2 may any amino acid or where X_1 may be conservatively modified variants of valine or where X_2 may be conservatively modified variants of glutamine. Claim 5 is drawn to a peptidomimetic of DXCXD. Claim 10 is drawn to a glycosylated polypeptide of claim 1. Claims 40-52 are drawn to fusion polypeptides comprising a polypeptide comprising the sequence DX_1CX_2D, where X_1 or X_2 may any amino acid. For claims 40-44 the fusion protein is

a fusion of a polypeptide having the sequence DXCXD in combination with a cell targeting moiety.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The specification teaches that Saposin B exhibits anti-angiogenic acitivity, which is mediated via inhibition of endothelial cell migration and endothelial cell proliferation (shown in Figures 1 and 2). The specification also demonstrates that peptide that are fragments of full length Saposin B, peptides having SEQ ID NO: 19 and SEQ ID NO: 28, where the fragments minimally comprise the sequence DVCQD, are able to inhibit endothelial cell proliferation (Tables 7 and 8) and that SEQ ID NO: 19 is also able to inhibit endothelial cell migration (Table 6). However, the specification fails to provide any examples where the second and fourth amino acids (the valine (V) and the glutamine (Q) of DVCQD) are substituted at the same time. The specification does provide examples where one or the other of the valine or glutamine is substituted, but the data does not appear to support the contention that the valine and glutamine residues do not contribute to the antiproliferative activity of the peptide DVCQD. In only one case, where the peptide has the sequence DVCDD, is the activity maintained. All other instances of substitution appear to result in a loss of activity, leading one to the conclusion that substitutions within the DVCQD sequence cannot be made predictably. Therefore, it appears

from the data provided in the specification that for the peptides to be useful for the methods described in the specification, the peptides must minimally contain the sequence DVCQD.

For claims to satisfy the enablement requirement of 35 U.S.C. 113, 1st paragraph, the specification must provide one of skill in the art with teachings for how to both make and to use the claimed inventions. In the instant case, the claimed polypepties appear to be intended for the use of inhibiting angiogenesis, either in the form of the polypeptide itself or in the form of a targeted polypeptide (fusion polypeptides). However, the claimed polypeptides encompass peptides that would not inhibit either the migration or proliferation of endothelial cells. Therefore, one of skill in the art would not be enabled for the full scope of the invention, because the one of skill in the art would not know what to use the great majority of the claimed species of polypeptides that are encompassed by the claims.

8. Claims1-3, 6-8, 10, 29-34, and 36-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to provide an adequate description of the genus of polypeptides comprising the sequence DXCXD, or the genus of polypeptides comprising the sequence of DXCXD, where this genus of polypeptides has anti-angiogenic acitivty.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed "polypeptides comprising a contiguous amino acid sequence DX_1CX_2D, where X_1 and X_2 are selected from the group consisting of amino acids", because the term comprising includes undescribed portions on either side of DXCXD. Also the skilled artisan cannot envision the detailed chemical structure of the encompassed "polypeptides comprising a contiguous amino acid sequence DX_1CX_2D, where X_1 and X_2 are selected from the group consisting of amino acids, and said polypeptide has antiangiogenic activity" that are used in the methods claims, are comprised within pharmaceutical compositions or are comprised within fusion proteins. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of manufacturing or testing the claimed process. As discussed above in the scope of enablement rejection for the broad polypeptide claims, the specification contains no examples of polypeptides where the DVCQD motif has been substituted in both the V and the Q positions. The specification does provide some examples where one or the other substitution has been made, but only one of those examples results in a peptide that maintains the same degree of activity as the parent (DVCQD) peptide. Therefore, the specification only provides two examples, DVCQD and DVDDD, that are within the scope of the claimed genus of peptides that are to be used or comprised within the claimed inventions. These two examples are not representative of the broadly claimed genus in view of the fact that

either of the two or both of the V and Q amino acids may be substituted. Therefore, the genus encompasses polypeptides containing hundreds of species of 5 amino acid motifs. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fides v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

9. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to provide an adequate description of the genus of peptidomimetics of DX_1CX_2D (where X1 and X2 are selected from the group consisting of amino acids.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed "peptidomimetics of peptide DX_1CX_2D, where X_1 and X_2 are selected from the group consisting of amino acids". Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of manufacturing or testing the claimed process. In the instant case, the specification provides no examples of "peptidomimetics". The only reference in the specification for the term "peptidomimetic" is as an example the scope of the terms "polypeptide", "peptide" and "protein" on page 15, lines 15-19, where a peptidomimetic appears to be a compound that that contains an" artificial chemical analog" of amino acids. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fides v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-6, 8, 9, 11-23 and 37-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Hammerstedt (U.S. Patent 5,910,568; issued June 8, 1999; effective filing date Jan. 11, 1996; cited in the IDS).

Claims 1-6 and 8, 9, 11-23 are drawn to polypeptides that comprise either DXCXD or DVCQD, and may have a length of between 5 and 71 amino acids, or because some of the independent claims encompass more than 71 amino acids may have a length that is either at least 518 amino acids in length or about 80 amino acids in length. Claims 37-39 are drawn to pharmaceutical compositions.

Hammerstedt teaches polypeptides with the sequences of SEQ ID NO: 4 and SEQ ID NO:5, which are polypeptides that comprise the sequence DVCQD and which are 15 amino acids and 19 amino acids in length, respectively. Hammerstedt also teaches SEQ ID NO: 15, which comprises the sequence DVCQD and which is 80 amino acids in length and has the specific amino acids in the positions indicated in claims 12-22. The polypeptide of SEQ ID NO: 15 of Hammerstedt also comprises the polypeptide sequence of SEQ ID NO: 19 of claim 23, and therefore, because of the fact that the phrase "about 71 amino acids" appears to include polypeptides having 80 amino acids, reads on the polypeptide of claim 23. Hammerstedt also teaches pharmaceutical compositions that may be considered to be a topical ointment (interpreted as a pharmaceutical preparation applied locally), because Hammerstedt teaches pharmaceutical preparations that may be administered near the cervical os (col. 6, lines 16-31).

11. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens (Stevens, R.L. et al. Biochemistry 32: 4051-4059, 1993).

Claims 1 and 10 are interpreted to read on a glycosylated peptide that comprises the sequence DXCXD. Stevens teaches a 79 amino acid peptide that comprises DXCXD (referred to as CS-Act [Cerebroside Sulfate Activator]) and teaches that it is glycosylated (see page 4056, Figure 4 and 2nd col., 2nd para). Thus, Stevens teaches a peptide that is the same as that claimed.

12. Claims 29, 30, 33-35, 37, 40, and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Katz (U.S. Patent 5,716,614); issued Feb. 10 1998; effective filing date Aug. 5, 1994) as evidenced by Stevens (supra).

Claims 29, 30 and 33-35 are drawn to methods of treating a mammal comprising administering an amount of a polypeptide comprising DXCXD (wherein such peptide may be Saposin B (CS-Act)). Because of the lack of antecedent basis for "said organism", the claimed methods are not limited to methods of administering to a mammal having a disease associated with angiogenesis. The administration may be intralesional or transdermal. Claim 37 is drawn to a pharmaceutical composition. Claims 40 and 41 are drawn to fusion proteins comprising a polypeptide having the sequence DXCXD.

Katz teaches peptide conjugates, pharmaceutical compositions and methods of treatment comprising the administration of Saposin B (see Table 2 in col. 12, line 14) for the treatment of Metachromatic leukodystrophy. Stevens provides the evidence that the enzyme listed by Katz in Table 2 (sulfatide activator/saposin) refers to Saposin B (also referred to as CS-Act) on page 4057, col. 1, where it is taught that the disease of Metachromatic leukodystrophy is caused by a deficiency in CS-Act. Katz teaches administration of directly into the brain parenchema, which reads on intralesional administration. Katz teaches fusion proteins where the targeting moiety is

a protein such the C fragment of tetanus toxin, alpha bungarotoxin or nerve growth factor. Thus, Katz teaches methods, pharmaceutical compositions and fusion proteins that are the same as those claimed.

13. Claims 1, 2, 5 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean (U.S. Patent 5,888,474; issued Mar. 30, 1999, 1999; effective filing date Jul. 11, 1994).

Dean teaches a labeled peptide that comprises the sequence DVCGD (SEQ ID NO: 27) and is 10 amino acids in length. Therefore, Dean teaches peptides that are the same as that claimed.

14. Claims 1, 5 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Tripp (U.S. Patent 5,639,876; issued Jun. 17, 1997; effective filing date Aug. 19, 1993).

Tripp teaches a peptide that comprises the sequence DDCGD (SEQ ID NO: 5) and is 9 amino acids in length and that may be glycosylated (see col. 6, lines 30-40). Therefore, Tripp teaches a peptide that is the same as that claimed.

15. Claims 1, 5 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Luster (U.S. Patent 6,403,782; issued Jun. 11, 2002; effective filing date Sep. 1, 1995).

Luster teaches a polypeptide that comprises the sequence DICAD (SEQ ID NO: 25) and is 74 amino acids in length (74 amino acids is interpreted to within the scope of "about 71 amino acids") and that may be glycosylated (see col. 6, lines 35-37). Therefore, Luster teaches a polypeptide that is the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
May 19, 2004

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER